Evidence base for opioid pharmacotherapy: methadone and buprenorphine

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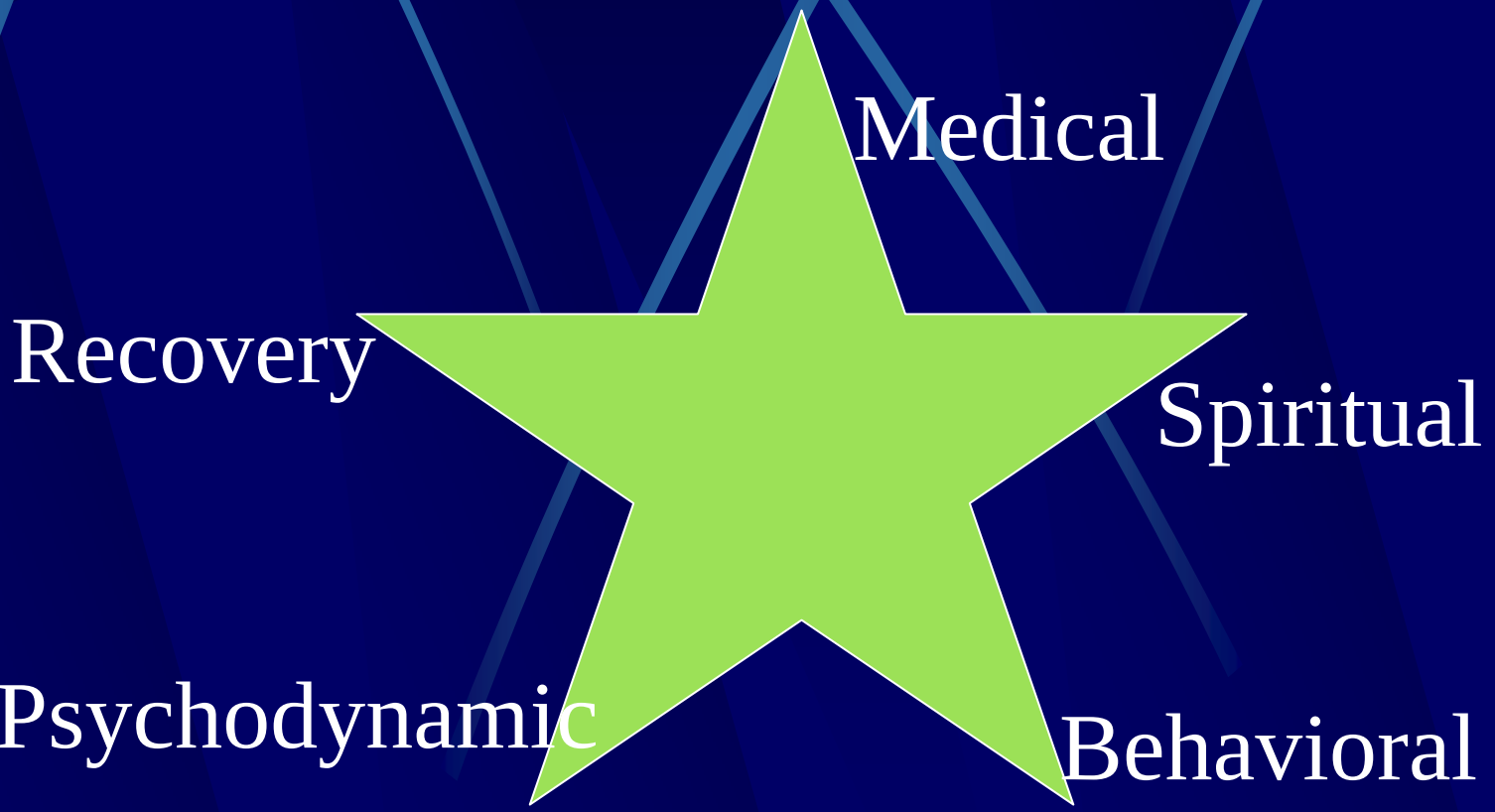
Talking to patients about addiction treatment models



Opioid abuse

Prevalence

- 3,744,000 persons in US reported using heroin at least once in their lifetime (2003 NSDUH)
- 149,000 new users (1999)
- 980,000 persons using heroin at least weekly (1998)
- 810,000 to 1,000,000 chronic users of heroin (ONDCP 2003)

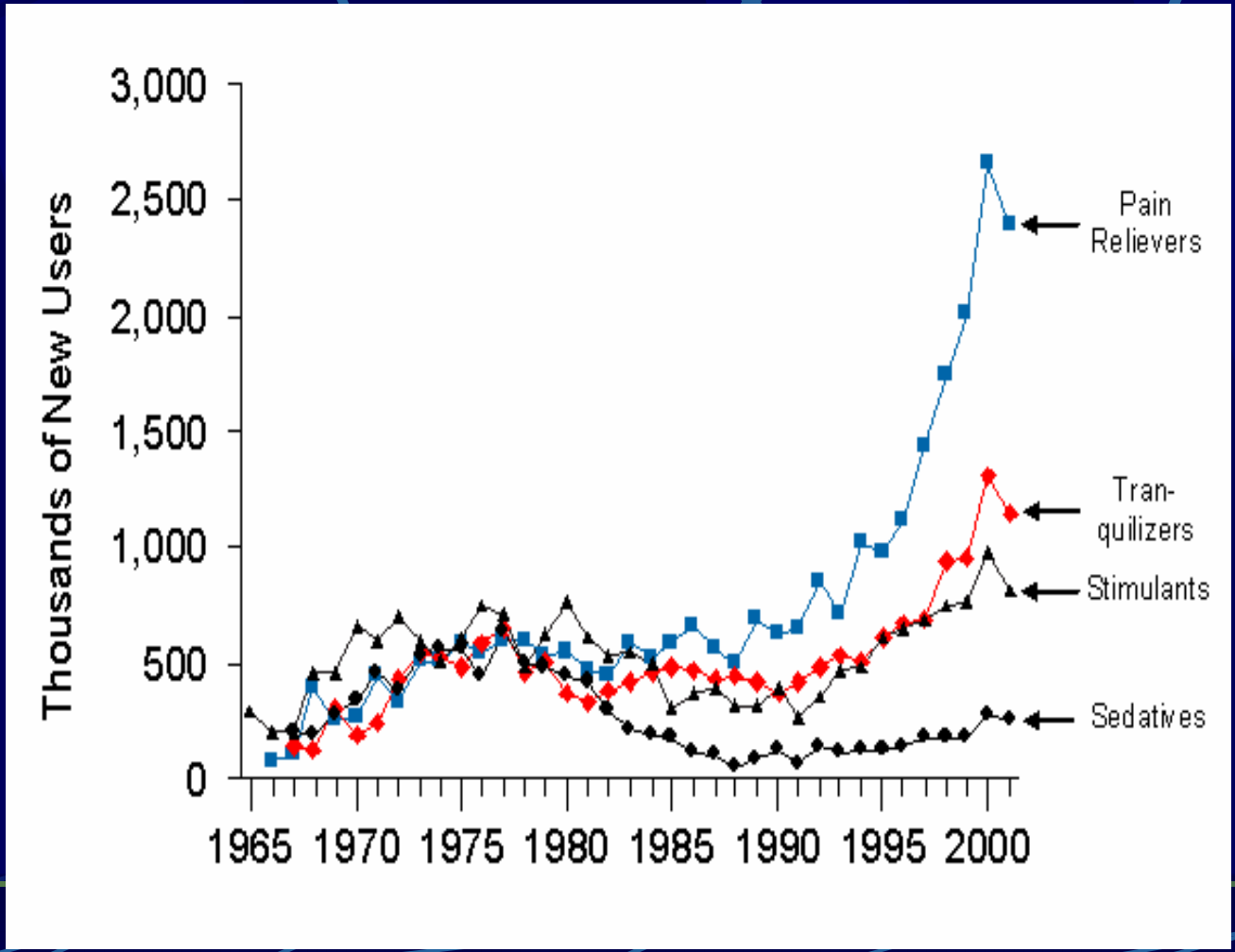
Gaps in current treatment of opioid dependence

810,000 to 1,000,000 chronic users of heroin

200,000± patients receiving methadone maintenance treatment

1998 NIH Consensus Statement on Appropriate Treatment of Opiate Dependence called for increased access to pharmacotherapy.

Number of new non-medical users of therapeutics



(NSDUH, 2002)

Commonly Abused Opioids

- Diacetylmorphine (Heroin)
- Hydromorphone (Dilaudid)
- Oxycodone (OxyContin, Percodan, Percocet, Tylox)
- Meperidine (Demerol)
- Hydrocodone (Lortab, Vicodin)

Commonly Abused Opioids (continued)

- Morphine (MS Contin, Oramorph)
- Fentanyl (Sublimaze)
- Propoxyphene (Darvon)
- Methadone (Dolophine)
- Codeine
- Opium

ADDICTION AS A CHRONIC ILLNESS

Chronic relapsing condition
which untreated
may lead to severe complications
and death.

ADDICTION AS CHRONIC DISEASE: IMPLICATIONS

- It is treatable but not curable.
- Adjustment to diagnosis is part of patient's task.
- There is a wide spectrum of severity.
- Retention in treatment is key.
- Best treatment is integrated.

Legally two types of opioid pharmacotherapy allowed:

- Methadone maintenance in specially licensed facilities
- Office-based treatment with buprenorphine.

Methadone maintenance:

- Evidence-based MAT since 1965.

Counseling Staff

THE DOSING WINDOW

Four questions patients ask:

- How is methadone better for me than heroin?
- What is the right dose of methadone for me?
- How long should I stay on methadone?
- What are the side effects of methadone?

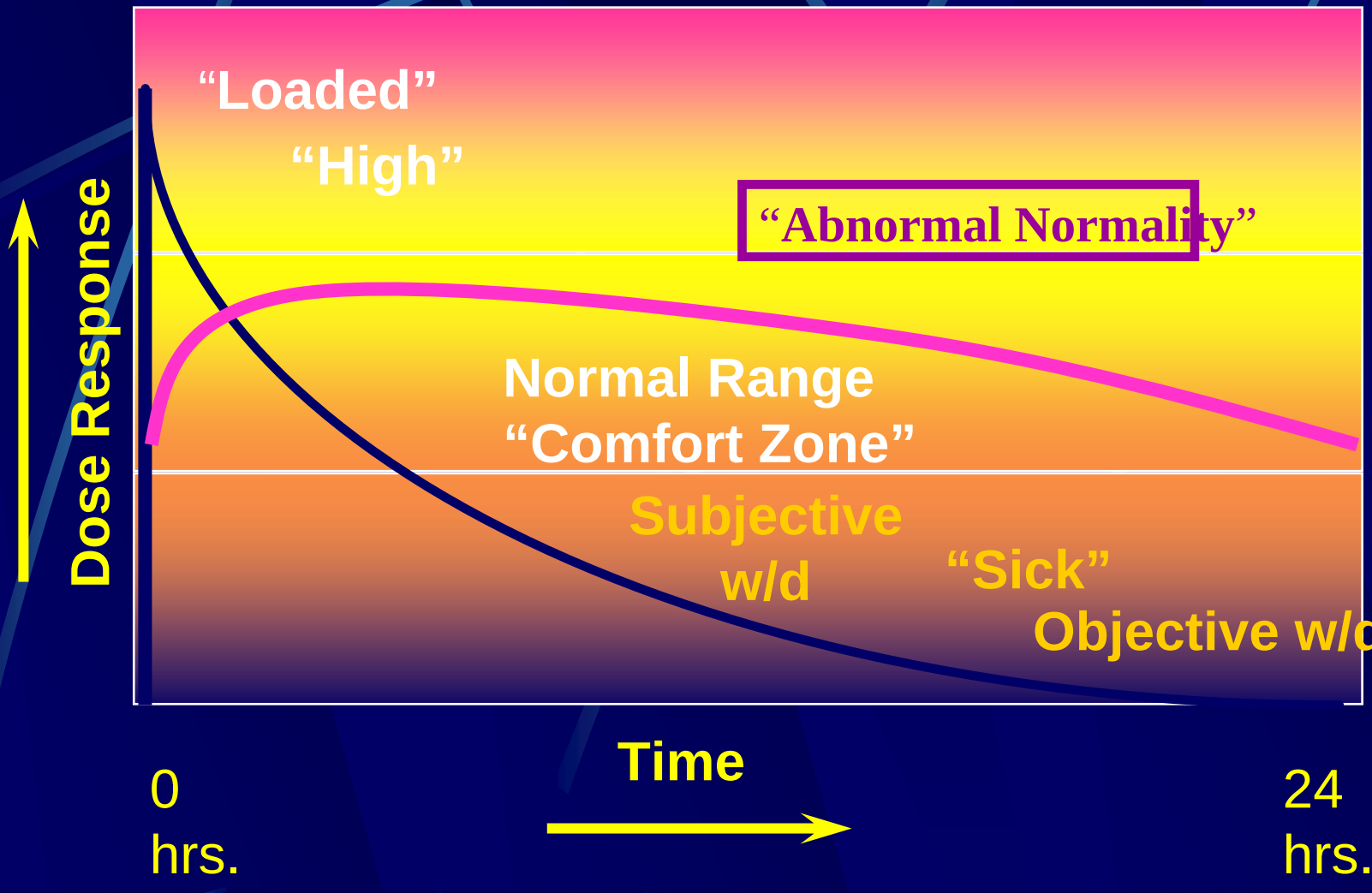
How is methadone better than heroin?

- Legal
- Avoids needles
- Known amount ingested

Opiate effects, physical

- Predictable physical effects of administering opiates:
  - **Tolerance**: the body becomes efficient in processing the drug and requires ever higher doses to produce the desired effect.
  - **Dependence**: when the drug is discontinued there are typical withdrawal signs and symptoms.

Methadone Simulated 24 Hr. Dose/Response
At steady-state in tolerant patient



How is methadone better than heroin?

- Legal
- Avoids needles
- Known amount ingested
- Slow onset: no “rush”
- Long acting: can maintain “comfort” or normal brain function
- Stabilized physiology, hormones, tolerance

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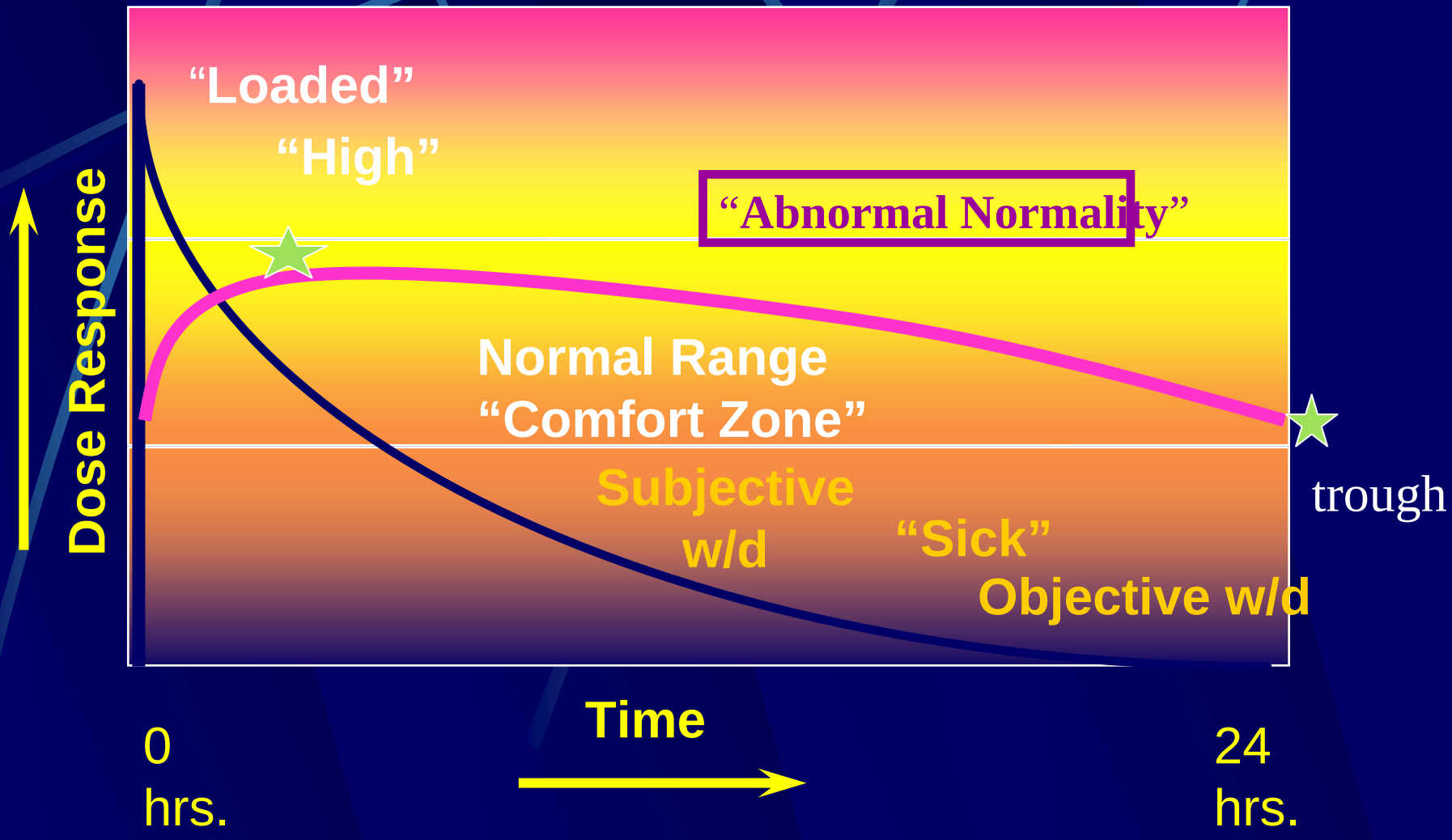


What is the right dose?

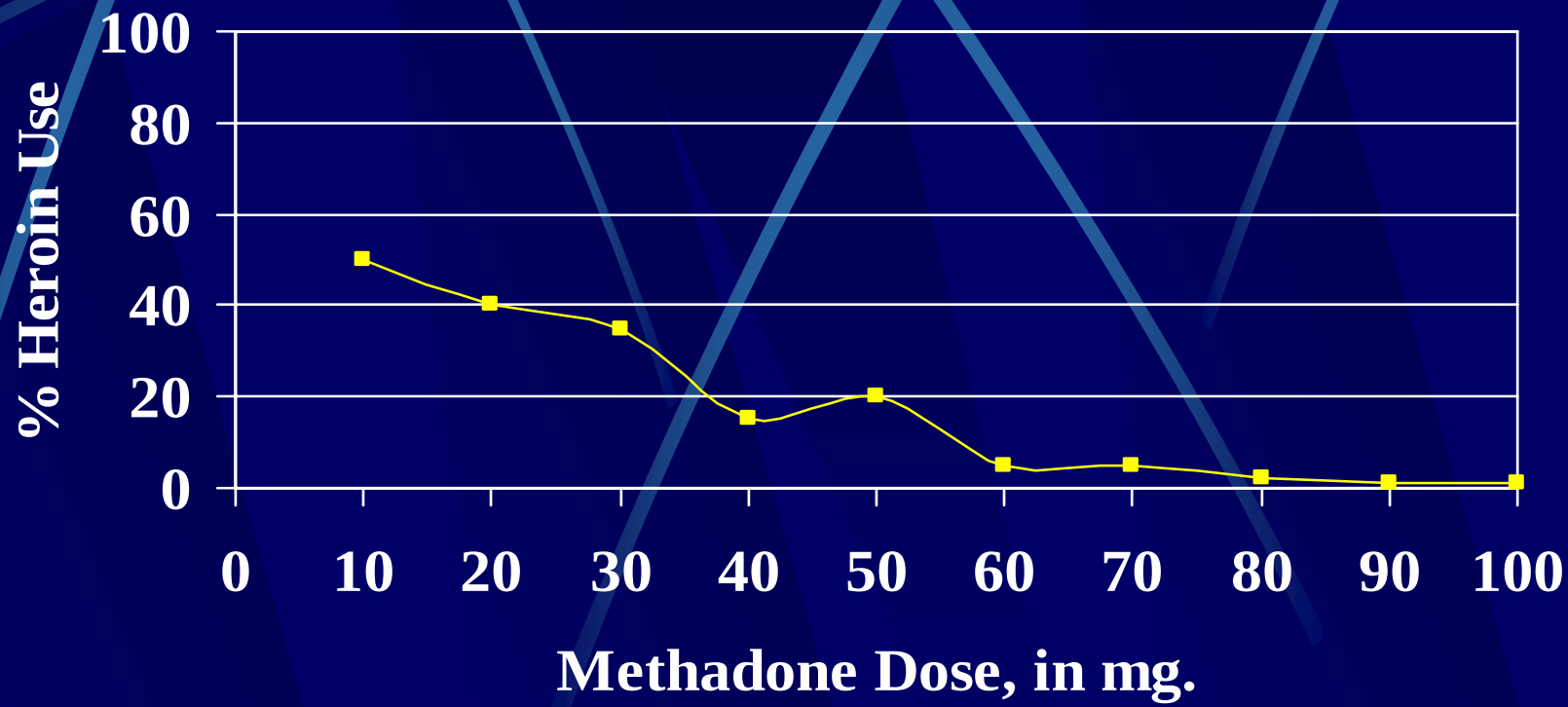
- Eliminate physical withdrawal
- Eliminate ‘craving’
- Comfort/function: usually trough is 400-600 ng/ml, peak no more than twice the trough.
- Not over-sedated
- Blocking dose

“How Much????

Enough!!!”

Tom Payte, MD

Recent Heroin Use by Current Methadone Dose



Ref: J. C. Ball, November 18, 1988
Slide adapted from Tom Payte

Four questions patients ask:

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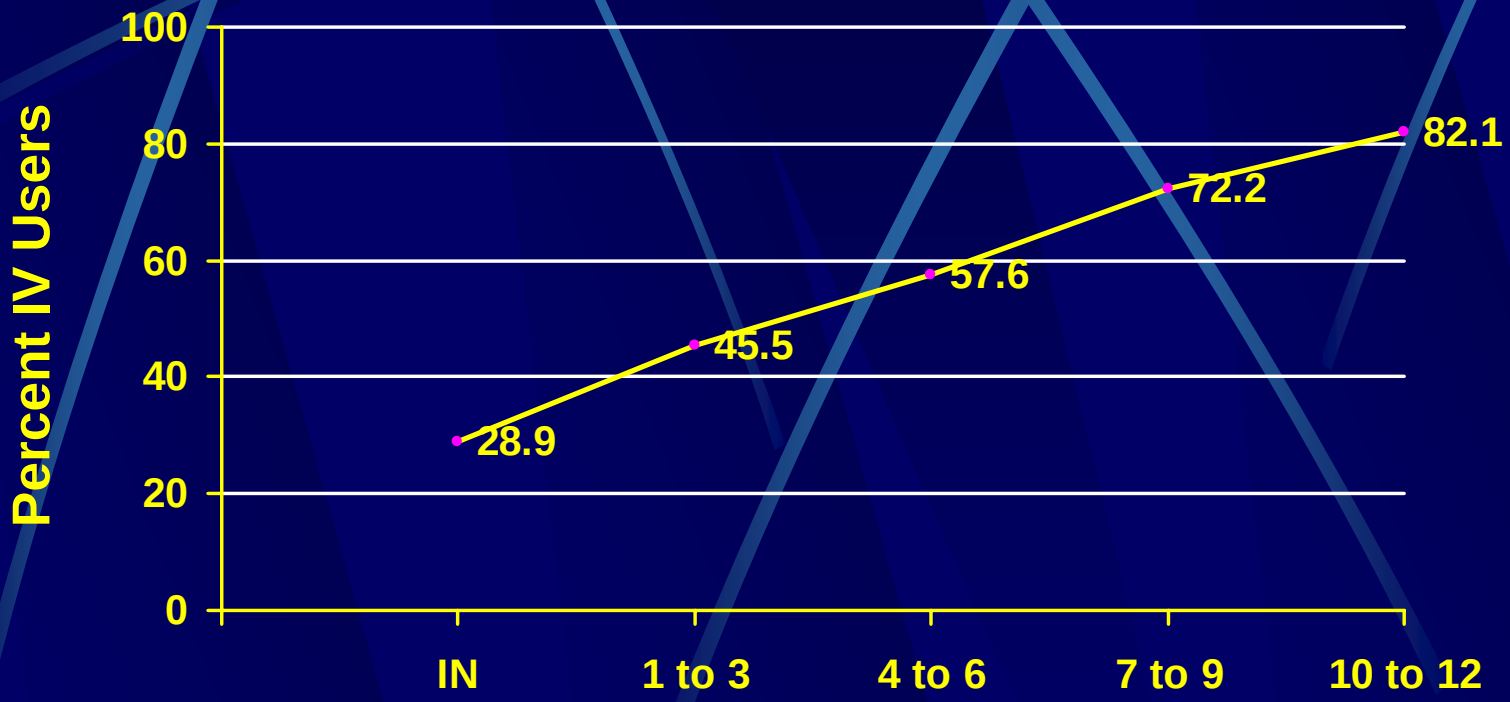
Relapse to IV drug use after MMT
105 male patients who left treatment



Adapted from Ball & Ross - *The Effectiveness of Methadone Maintenance Treatment*, 1991

“How Long???

Long Enough!!”

Tom Payte, MD

Four questions patients ask:

- How is methadone better for me than heroin?
- What is the right dose of methadone for me?
- How long should I stay on methadone?
- ***What are the side effects of methadone?***

Side effects of methadone:

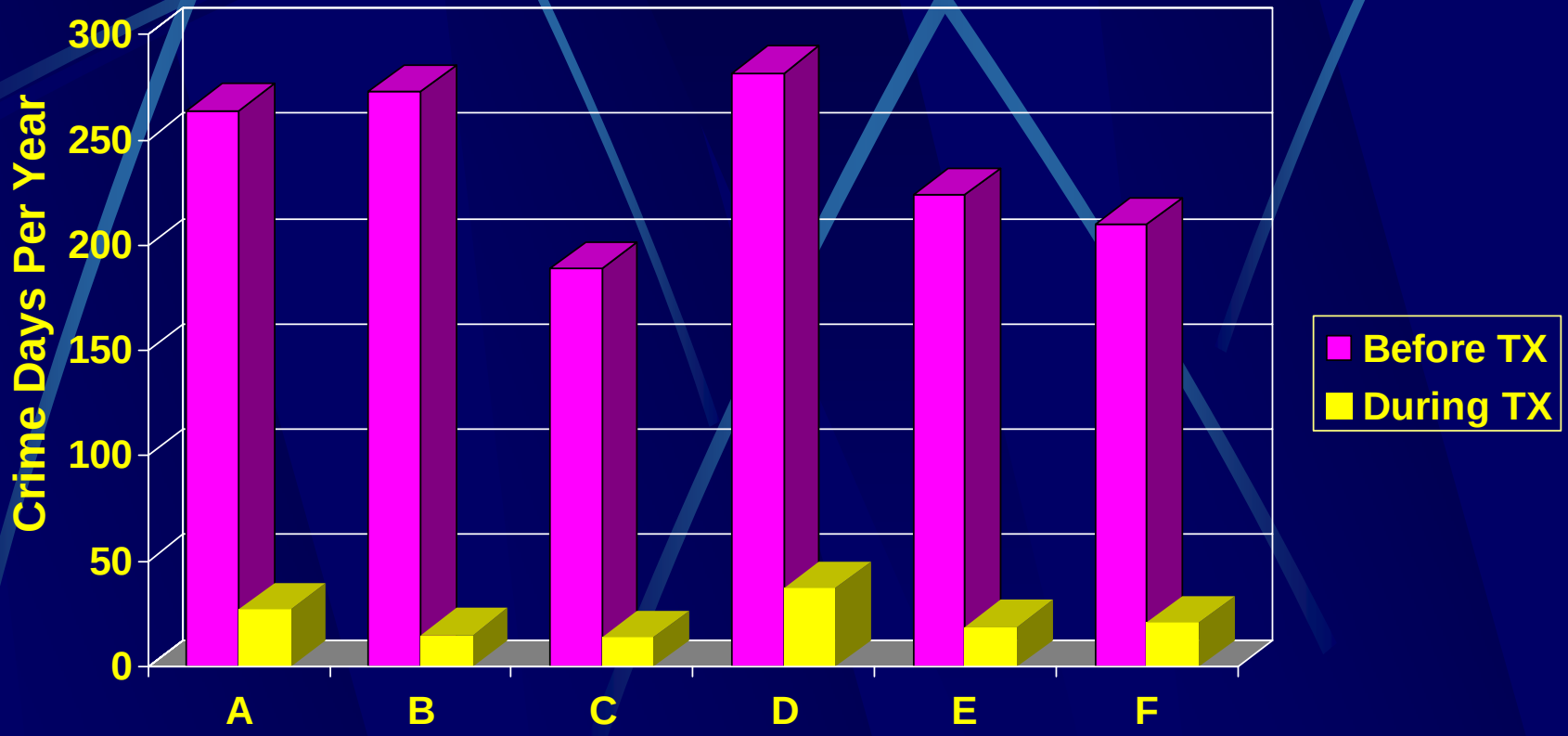
- General opiate effects:
  - Sedation/stimulation
  - Maintained phys. dependence (stable)
  - hypogonadism (not as severe as with heroin, may be dose dependent)
- Constipation
- Slight QTc prolongation on ECG (Martell etal)
- Sweating
- Methadone treatment tied to regulated clinic

Treatment Outcome Data

- 4-5 fold reduction in death rate
- reduction of drug use
- reduction of criminal activity
- engagement in socially productive roles
- reduced spread of HIV
- excellent retention

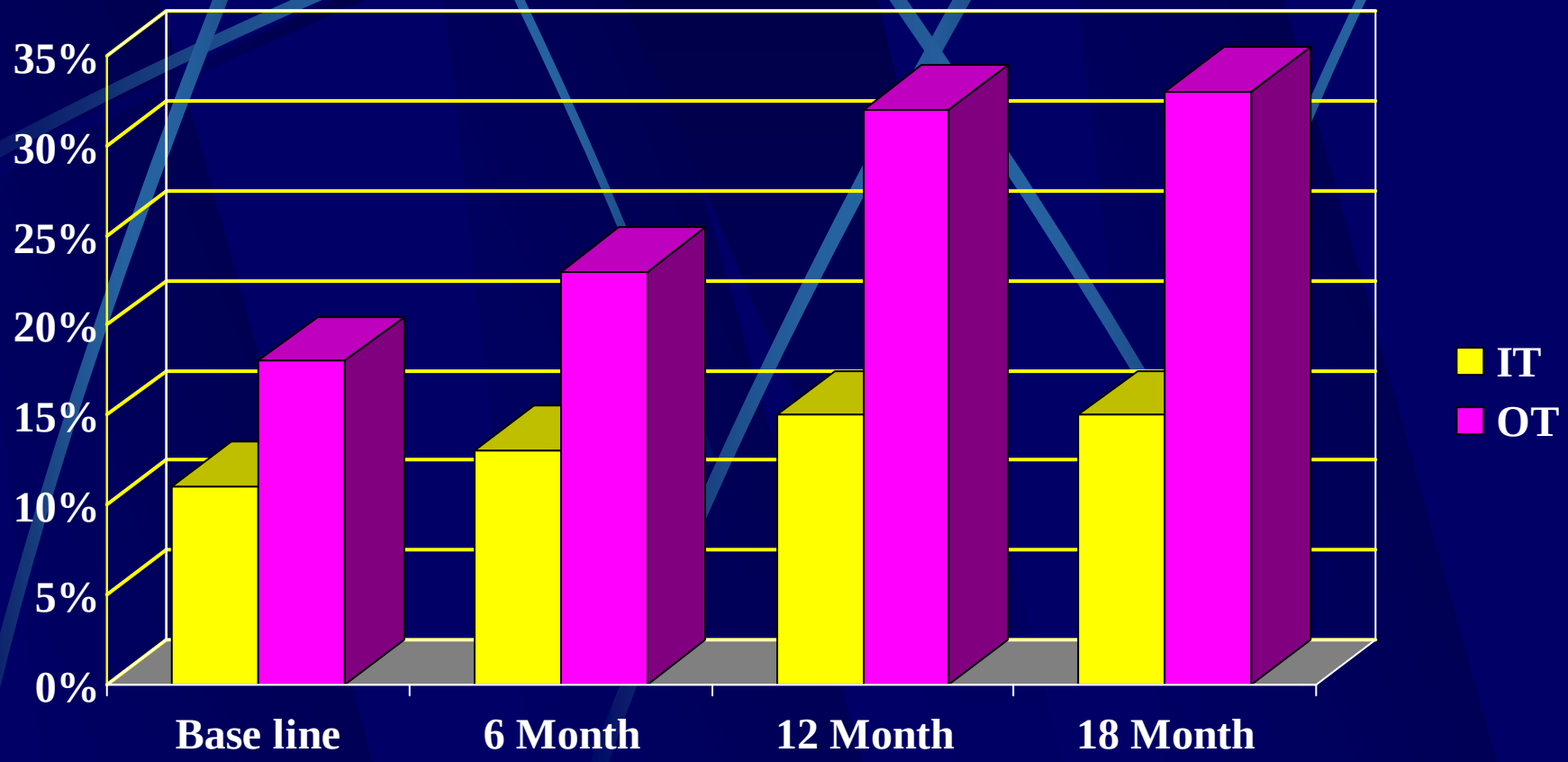
(see: Joseph et al, 2000, Mt. Sinai J.Med., vol67, # 5, 6)

Crime among 491 patients before and during MMT at 6 programs



Adapted from Ball & Ross - The Effectiveness of Methadone Maintenance Treatment, 1991

HIV CONVERSION IN TREATMENT



HIV infection rates by baseline treatment status. In treatment (IT) n=138, not in treatment (OT) n=88

Source: Metzger, D. et. al. J of AIDS 6:1993. p.1052

Other drugs of abuse: how do they affect MMT?

- Stimulants: patients do poorly
- Alcohol: additive sedation, complicate Hep C.
- Benzodiazepines: synergistic sedation
- THC: no effect on major outcomes
- Opioids: usually blocked, tolerance

Pregnancy

- MMT treatment of choice for pregnant, opioid-abusing women.
- Efforts to avoid intra-uterine fetal withdrawal, including split dose.
- Neonatal withdrawal occurs within 72 hours, at least 45% need treatment.
- Breastfeeding recommended if not HIV positive.

Pain in patients on MMT

- Methadone is prescribed for pain treatment in twice or three times daily doses.
- Up to 60% of MMT patients have chronic pain (Jamison 2000, Rosenblum 2003)
- Split doses may be indicated.

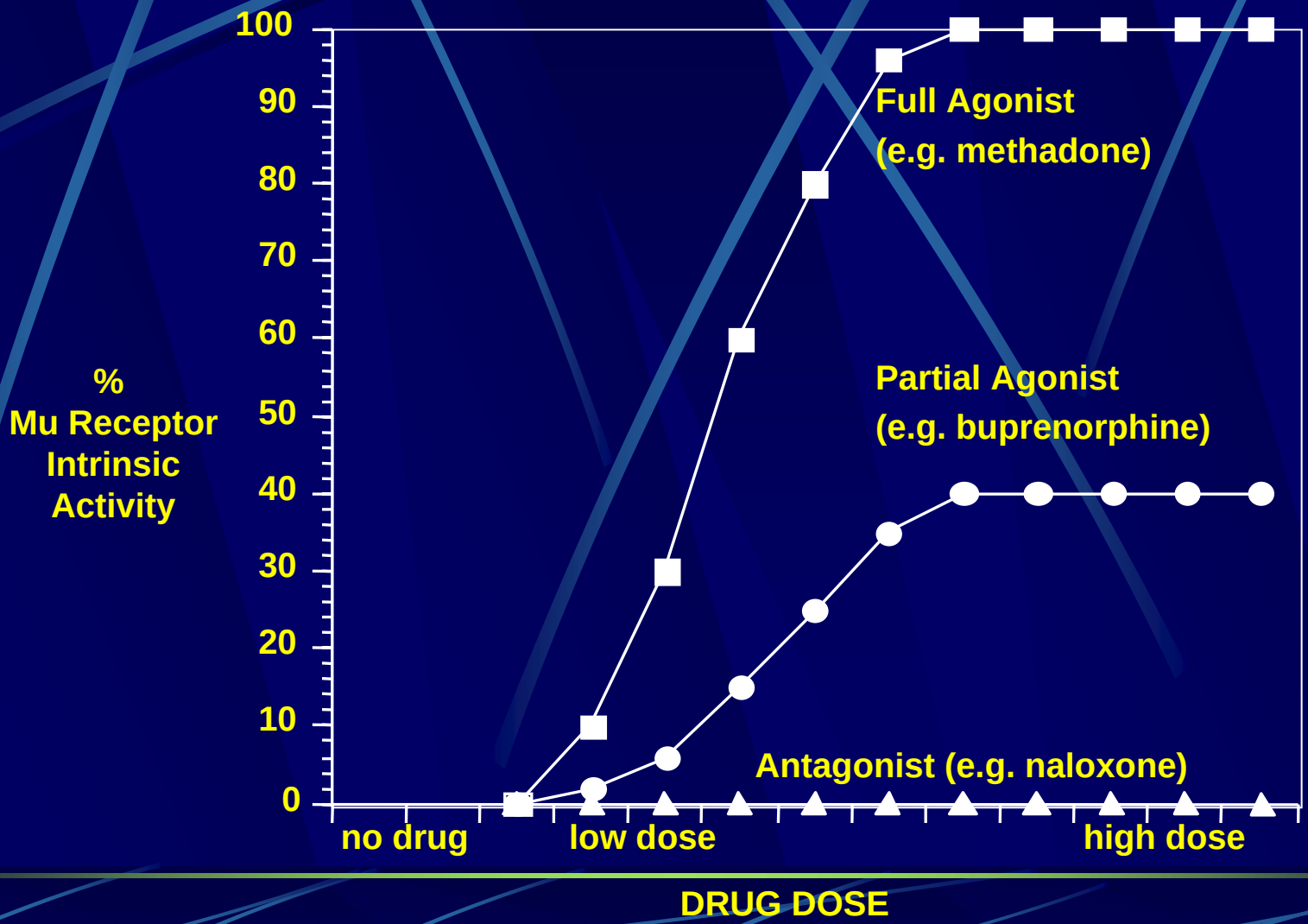
Drug Addiction Act of 2000 (DATA 2000)

- Allowed office-based treatment with opiate for opioid addicted patient with restrictions.
- Physicians may qualify by 8 hours of training
- Physicians notify HHS that they intend to prescribe

A FEW WORDS ABOUT BUPRENORPHINE

- “Ceiling effect” and safety
- Displaced other opiates: withdrawal on induction
- Sublingual tablet
- Schedule 3(methadone is 2)
- One form combined with naloxone
- Office – based use available

Comparison of Activity Levels



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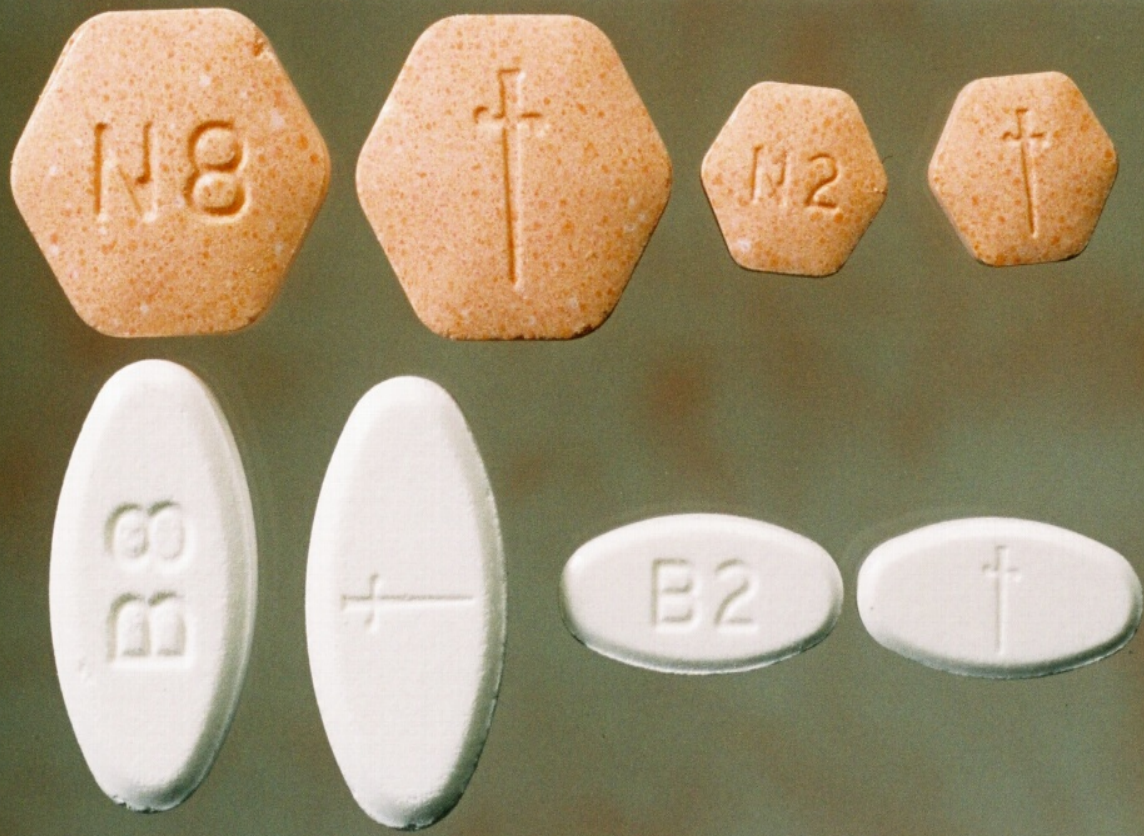

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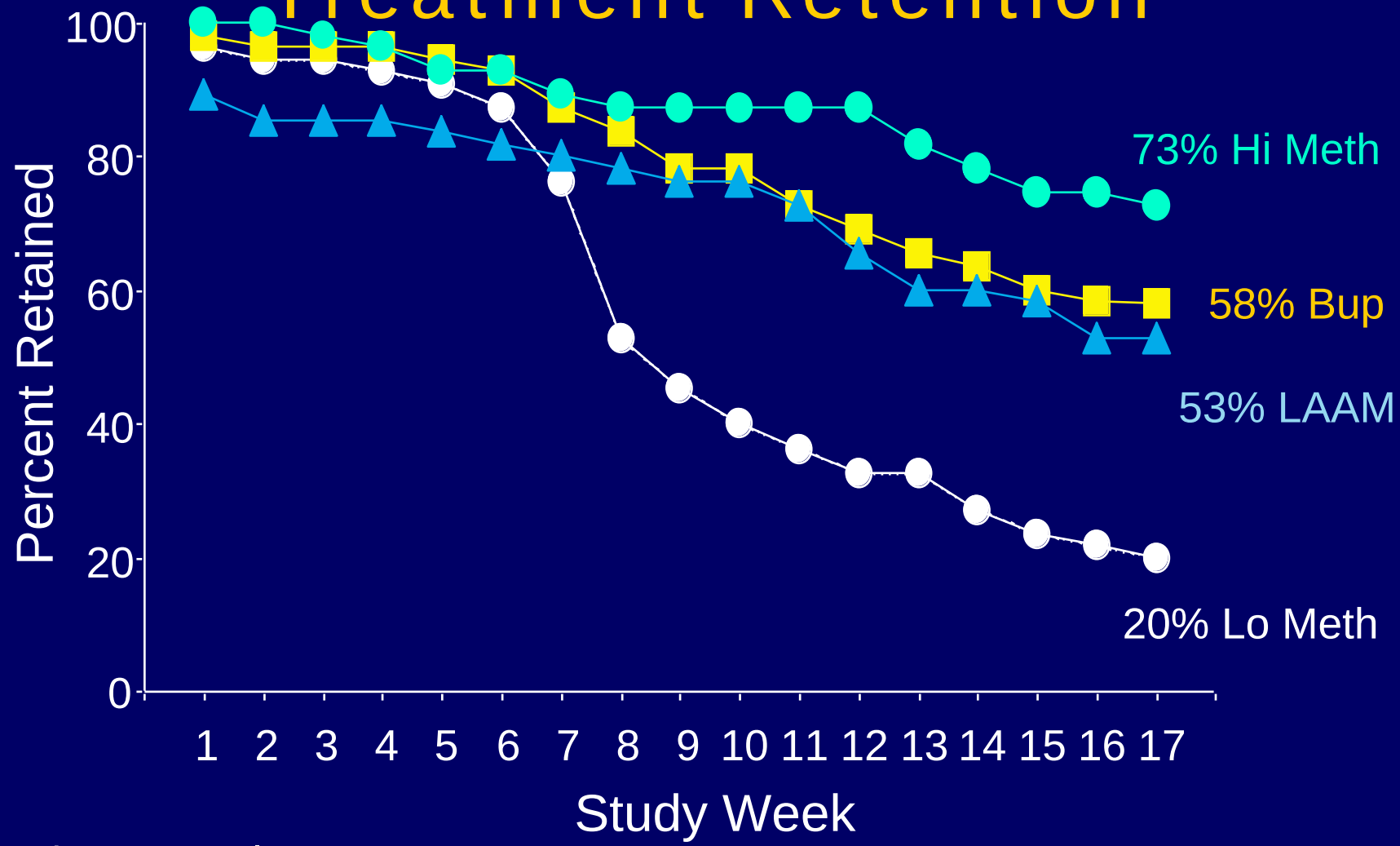
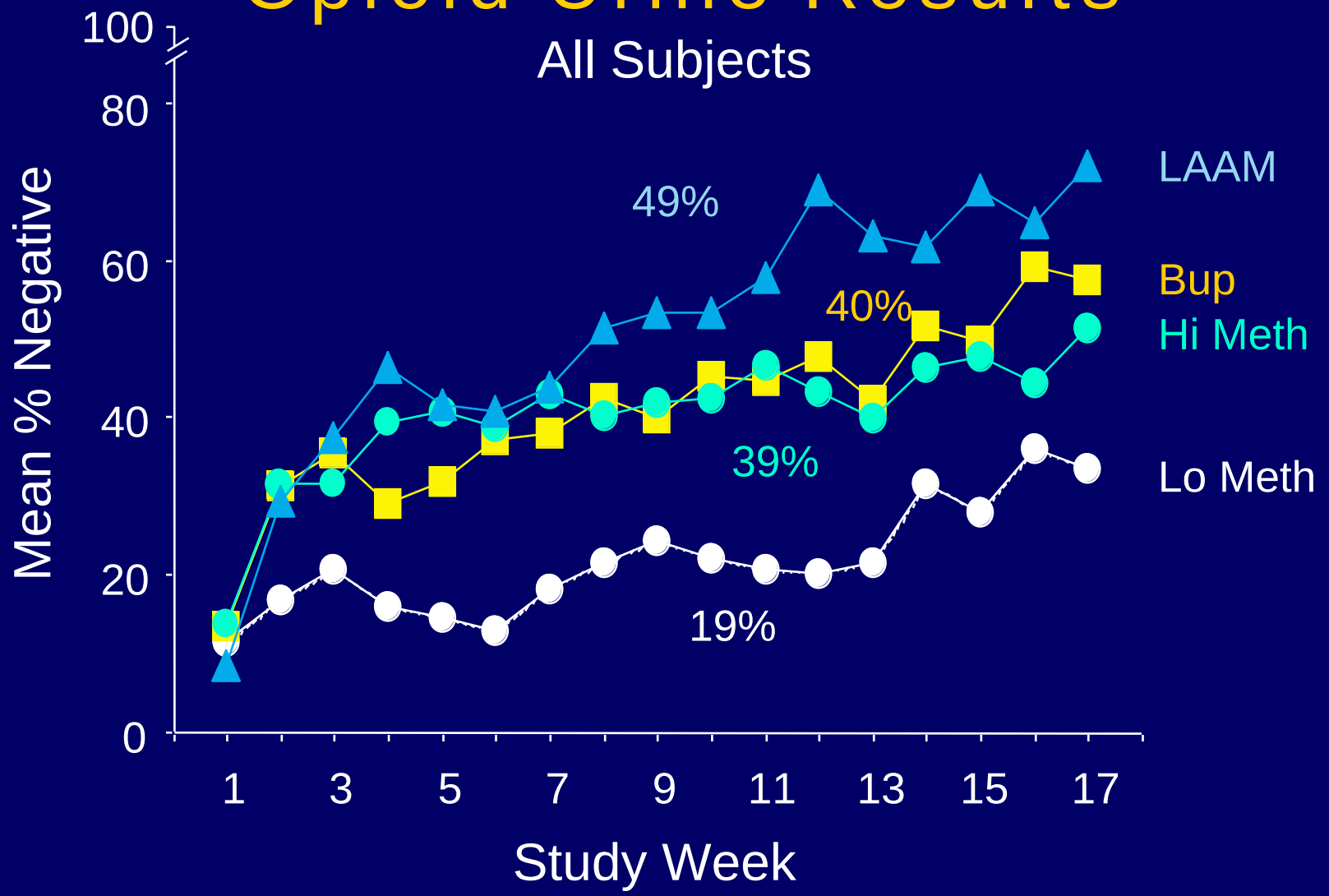
Buprenorphine, Methadone, LAAM: Treatment Retention



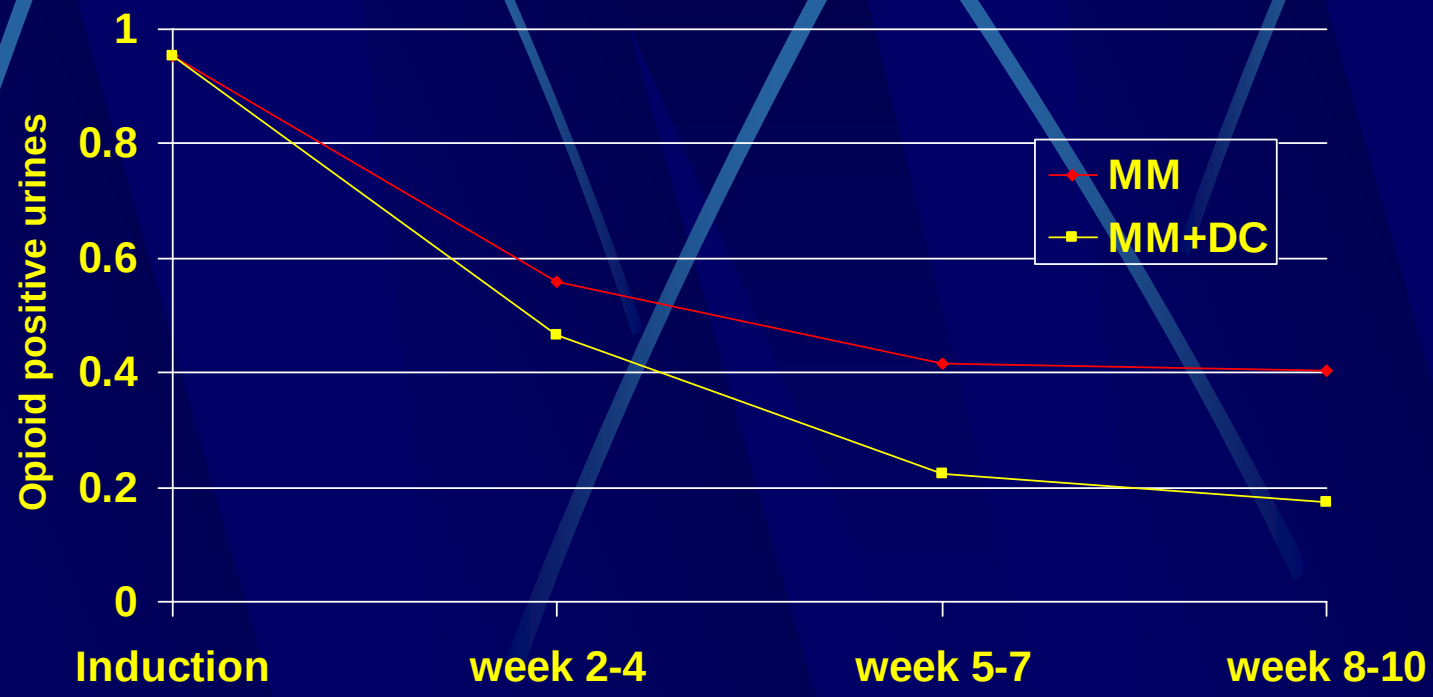
Johnson et al, 2000

Buprenorphine, Methadone, LAAM: Opioid Urine Results



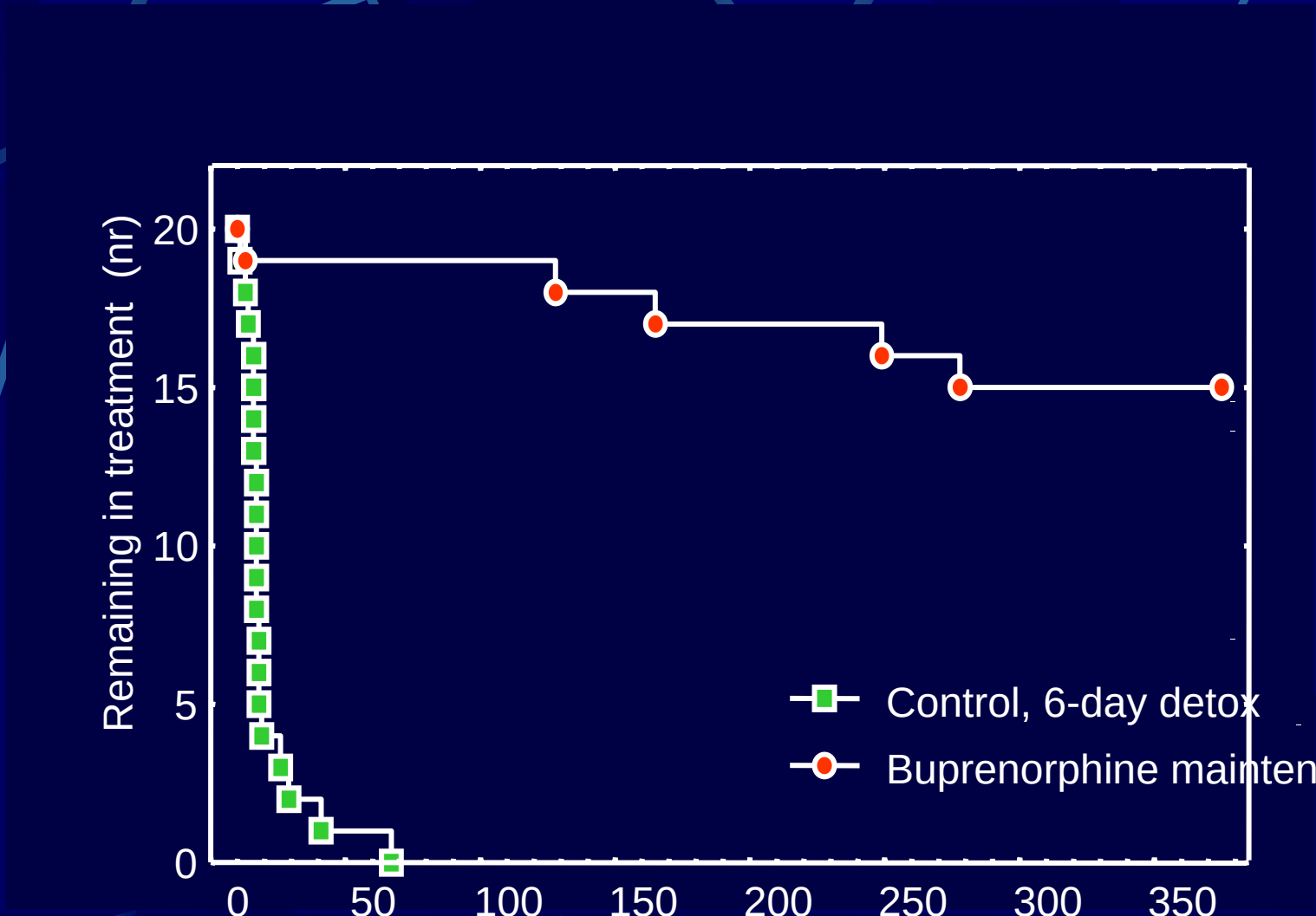
Effect of counseling in buprenorphine treatment

(Fiellin, 2002)



Retention in treatment

Kakko et al, 2003,



Pharmacotherapy in context: correct glossary

- Abstinence includes pharmacotherapy
- Maintenance, not substituion or replacement (new term also: MAT)
- Tapering from maintenance, not detoxification, (also ‘medically supervised withdrawal’, or MSW)
- Discontinuation, not discharge
- Toxicology screens: pos/neg, not clean/dirty)

Opioid pharmacotherapy, summary:

- Methadone, buprenorphine and LAAM all approved by the FDA for treatment of opiate dependence. (LAAM not currently available from any drug company)
- Best evidence so far supports maintenance.
- Detoxification attempts should have maintenance as a back up in case of relapse.